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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/479,997	06/07/1995	DEAN ENGELHARDT	ENZ-5(D6)(C2	8799

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EXAMINER	
MARSCHEL, ARDIN H	
ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 11/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	08/479,997	ENGELHARDT ET AL.	
	Examiner	Art Unit	
	Ardin Marschel	1631	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 03 September 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1.☒ A Notice of Appeal was filed on *03 September 2004*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2.☒ The proposed amendment(s) will not be entered because:

(a) ☒ they raise new issues that would require further consideration and/or search (see NOTE below);

(b) ☒ they raise the issue of new matter (see Note below);

(c) ☒ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

(d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: *See attached explanation.*.

3.☒ Applicant's reply has overcome the following rejection(s): See Continuation Sheet.

4.☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5.☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *of reasons record which are dicussed further as attached*.

6.☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7.☒ For purposes of Appeal, the proposed amendment(s) a)☒ will not be entered or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____.

Claim(s) objected to: _____.

Claim(s) rejected: *826-1227*.

Claim(s) withdrawn from consideration: _____.

8.☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9.☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10.☐ Other: _____

Continuation of 3. Applicant's reply has overcome the following rejection(s): The 35 USC 112, 2nd para., rejn. over nucleotide analog metes and bounds.

DETAILED ACTION

Explanation of new issues regarding item # 2 on the enclosed Advisory action:

The following new issues in the proposed claims, filed 9/3/04, would require further consideration and/or search.

In claim 826, proposed 9/3/04, line 14, the insertion of the phrase "comprising at least three carbon atoms" adds the new issues of both NEW MATTER and vagueness and indefiniteness. In lines 13-14 of claim 826, the Sig moiety was previously claimed as comprising a "non-peptidyl...label moiety" and claim 827 further limited the Sig as comprising at least three carbon atoms. As inserted in claim 826, the phrase "comprising at least three carbon atoms" may be confusingly interpreted as only modifying the "label moiety", thus defining the carbon atom content thereof, or, alternatively, modifying the "Sig" entity which further also comprises said label moiety. These two interpretations are different as to what specifically is limited regarding carbon atom content since the Sig moiety comprising said label moiety is interpreted via the "comprising" wording to at least containing the label moiety but also optionally containing more than the label moiety. It is noted that claim 827 which has been proposed as being canceled clearly was set forth previously as limiting the Sig entity content and not the label moiety therein. The above carbon atom limitation now being applied to the label moiety as an option is therefore NEW MATTER. This added NEW MATTER and added vagueness and indefiniteness is also present in proposed independent claims 856, 888, 921, 956, 988, 1022, 1054, 1088, 1121, 1156, and 1191;and claims dependent therefrom; as well as claim 826, due to their dependence.

In claim 826, proposed 9/3/04, lines 15-16, the added phrase "or modified nucleotide analog" adds the new issue of NEW MATTER, and/or new limitation issue, of such a modified nucleotide analog as now being itself incorporated in the "said oligo- or

polydeoxyribonucleotide". This new issue is indicative of the claimed oligo- or polydeoxynucleotide also additionally having an incorporated "modified nucleotide analog" over that what already comprises "said oligo- or polydeoxyribonucleotide". This requirement for a second such modified nucleotide analog is a new issue that would require further consideration and/or search regarding such incorporation per se practice which was not previously presented as claimed. This added NEW MATTER, and/or new limitation issue, is also present in proposed independent claims 856, 888, 921, 956, 988, 1022, 1054, 1088, 1121, 1156, and 1191; and claims dependent therefrom; as well as claim 826, due to their dependence.

Another new issue that would require further consideration and/or search is the improper amending status identifiers utilized in the proposed amendment, filed 9/3/04. Numerous claims, such as claim 829, cite the identifier, "(Previously Added)", which is not one of the accepted identifiers. Instead of this improper identifier, "(Previously Presented)" seems to have been the proper form.

Further explanation of item # 5 on the enclosed Advisory action:

The NEW MATTER rejection of claims 826-1227 based on the added limitation phrase "non-nucleotidyl" is maintained and reiterated from the previous office action, mailed 7/14/04, due both to the non-entry of the proposed amendment, filed 9/3/04, as well as for reasons of record.

Applicants argue that each citation of a Sig component as filed is not nucleotide or nucleotidyl in nature, citing several Sig citations such as enzyme, enzymic material, alkaline phosphatase, etc. In response none of these citations appreciate any nucleotide or nucleotidyl character for Sig, positive or negative, thus failing to provide written support for the limitation "non-nucleotidyl". Of particular interest is the citation of a polysaccharide, oligosaccharide, or monosaccharide which may be interpreted as

bridging over inclusively nucleotidyl as well as non-nucleotidyl Sig components. Thus, there is clearly no written description which appreciates any nucleotidyl Sig component subject matter limitation. Applicants also admit in their REMARKS, filed 9/3/04, that Sig is not described anywhere regarding being either nucleotidyl or non-nucleotidyl or not in nature. Applicants go on to argue that Sig is described in each instance as being a non-nucleotidyl component type. In response this is inconsistent with the fact that a polysaccharide Sig component as argued as noted above and also discussed above may be either nucleotidyl or not thus supporting this rejection in that there is no written limitation for only non-nucleotidyl Sig components to support such a claim limitation. Thus, applicants' argument that all Sig components are disclosed excluding non-nucleotidyl types is inconsistent with the factual basis as they themselves have argued and therefore non-persuasive. Applicants then argue that the specification on pages 94 and 95 cite nucleotides having a formula containing a Sig chemical moiety which would have been referred to as a dinucleotide at the very least. In response applicants have set forth as filed a variety of Sig components and would reasonably be expected to exemplify Sig in formula forms of components to be inclusive of all such Sig moieties as being generic. Applicants' argument that a dinucleotide would have been singled out to be separately a Sig containing component is an allegation as to what may or may not have been meant by Sig in such formula structures and lacks written basis for such a specific interpretation and therefore non-persuasive. Applicants then also allege that claim 141 demonstrates the "nucleotide" character of a claimed Sig containing compound as not being a dinucleotide or it would have been cited as such. In response applicants' again are alleging such an interpretation to the claim without factual or written support as filed. Additionally, it is noted that the Sig components argued by applicants include such types as enzymes, monosaccharide, amongst others. If

applicants would refer to an enzyme (Sig) – P – S – B structure as a nucleotide, then the Sig character is being ignored in such a construct as to specifically characterizing it as a nucleotide. Such a construct commonly would be called an enzyme/nucleotide conjugate in the art because of the significant content of an enzyme that would normally not be ignored due to its being larger generally in size and weight than the P – S – B portion of the entity. Thus, the nucleotide characterization argued by applicants in context clearly lacks any indication of what the content of Sig is as being enzyme, fluorescent entity, nucleotide itself, etc. This same response is appropriate for the remaining arguments of applicants which non-persuasively attempts to utilize the nucleotide naming of a Sig containing entity as excluding Sig being itself a variety of material types, nucleotidyl or not.

Lastly, a Declaration of Dr. Alex A. Waldrop, III, is set forth regarding this rejection. Consideration of said Declaration reveals that item 10 therein starts actual arguments regarding this rejection. In said item 10 the statement is made that none of the examples for the Sig label moiety are nucleotidyl or a nucleotide. In response it was noted above that the instant specification sets forth that polysaccharides, oligosaccharides, and monosaccharides are optional Sig moiety types, which are reasonably inclusive of nucleotide or nucleotidyl Sig types. Nucleotides are well known to be monosaccharides due to the ribose or deoxyribose content therein as part of their basic structure. Thus, the opinion expressed in said Declaration is contrary to the factual disclosure of such monosaccharide Sig moieties and thus non-persuasive.

In item 11 of said Declaration, the page 94 and claim 141 Sig moiety presence in described nucleotides is set forth. The nucleotide characterization of the Sig containing compound as not excluding nucleotide or nucleotidyl Sig types has been responded to

above as being a non-persuasive argument. The above response is reiterated here as being equally non-persuasive.

In item 12 of said Declaration, this same argument is argued regarding written basis of what is not described and is equally non-persuasive for the same reasons as for item 11 above.

In item 13 of said Declaration, citations from pages 95, 96, and 99 are also discussed regarding references to nucleotides with a Sig moiety. These citations are equivalent to the above item 11 citation which has been responded to above as being non-persuasive and are reiterated here as being equally non-persuasive because the Sig containing entities are clearly not being described with any particularity as to what such entities are named or conjugate naming etc. as appropriate would be expected to be utilized for Sig containing components which are complex. Thus, whether Sig is itself a nucleotide or nucleotidyl or not is not defined by Sig – PM – S – B being called a nucleotide.

Item 14 continues this argument with more examples which are equivalent to those argued above and are equally responded to as being non-persuasive.

Item 15 is a summary of previous arguments and an opinion, which as responded to above, is contrary to the facts disclosed in the specification as to lacking any specific nucleotidyl or non-nucleotidyl limitation regarding Sig. This Declaration is therefore non-persuasive regarding the above reiterated NEW MATTER rejection regarding the "non-nucleotidyl" limitation as in the pending claims.

The rejection of claims 855, 886, 920, 955, 987, 1020, 1053, 1086, 1120, 1154, 1188, and 1125 based on 35 U.S.C. 112, second paragraph, is maintained and reiterated from the previous office action, mailed 7/14/04, due both to the non-entry of the proposed amendment, filed 9/3/04, as well as for reasons of record.

If the amendment, proposed 9/3/04, had been entered; the vagueness and indefiniteness of dependent claims 855, 886, etc. regarding requiring a ribonucleotide and depending from a claim, respectively, being directed to deoxy-type oligomers or polydeoxynucleotides would have overcome this basis for rejection.

The scope of enablement rejection of claims 956-987 under 35 U.S.C. 112, first paragraph, is maintained and reiterated from the previous office action, mailed 7/14/04, due both to the non-entry of the proposed amendment, filed 9/3/04, as well as for reasons of record. If the amendment had been entered this rejection would have been overcome, however.

The rejection of claims listed as specified in the previous office action, mailed 7/14/04, based on 35 U.S.C. 102(a) as being clearly anticipated by Hartmann et al. [Biopolymers 20:2635 (1981)] is maintained and reiterated from the previous office action, mailed 7/14/04, due both to the non-entry of the proposed amendment, filed 9/3/04, as well as for reasons of record. Applicants only argued this rejection based on entry of the amendment, which if it were deemed to not contain NEW MATTER would have overcome this rejection.

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the Central PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The Central PTO Fax Center number is (703) 872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ardin Marschel, Ph.D., whose telephone number is (571) 272-0718. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (571) 272-0722.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instrument Examiner, Tina Plunkett, whose telephone number is (571) 272-0549.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

November 23, 2004

ARDIN H. MARSCHEL
PRIMARY EXAMINER